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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/683,264	12/05/2001	Michael A. Siani-Rose	3407.2	1024

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EXAMINER

MAHATAN, CHANNING

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/683,264	Applicant(s) SIANI-ROSE ET AL.	
	Examiner Channing S Mahatan	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11,20-30,39-49 and 82-105 is/are pending in the application.
- 4a) Of the above claim(s) 1-11,20-30 and 39-49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 82-105 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2 Sheets</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

REQUEST FOR CONTINUED EXAMINATION

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicants' submission filed on 29 November 2004 has been entered.

APPLICANTS' ARGUMENTS

Applicants' arguments, filed 29 November 2004, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 82-105. Claims 12-19, 31-38, and 50-81 have been canceled. Claims 1-11, 20-30, and 39-49 remain withdrawn as directed to a non-elected invention without traverse.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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NEW MATTER

New claims 82-105 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claims 82, 90, 98, and all claims dependent therefrom are rejected under 35 U.S.C. § 112 1st paragraph. Applicants' state in the response filed 29 November 2004 (page 9, lines 4-6) that:

"New claims 82-105 were added to more distinctly claim the invention. Support for the new claims can be found throughout in the specification. No new matter has been added."

However, this is not agreed with. The specification provides the following with respect to "automatically selecting a plurality of hits based on at least the plurality of scores and a plurality of criteria":

"A correspondence between a SCOP family and a gene was based on the E-value scored by SAM-T99. The program distsieve (attached computer program listing) examined all the sequences scored against a particular SCOP model. Because the interpretation of distance scores, expressed as logarithmic E-values was dependent upon the HMM generated for each sequence, there is no single E-value threshold that can be applied to all models. Instead, for each HMM, the distsieve method examined the set of scores by curve analysis to determine a reasonable E-value threshold. The distance scores included controls representing the proteins used to build all the models; thus, the best hit was often the seed sequence for the HMM.

Five criteria were used to distinguish the hits to be kept: (1) when the E-values rised above a value of e-05 they were discarded regardless of the other criteria; (2) the first ten hits were kept provided they score better than e-05; (3) the hits more than 70% of the log of the maximum score were automatically kept; (4) the point where the E-value plot drops abruptly or flattens was used as a threshold; (5) no more than a maximum number of hits (e.g., 1000) are kept.

Next, the set of hits accepted by distsieve were grouped by superfamily (806), where each gene is assigned to one SCOP family HMM according to the best distance score. While SAM-T99 was designed and optimized for superfamily recognition, GRAPA was designed for function prediction at the family level. Among the representative HMMs in the superfamily, the scores for each hit was compared and assigned to the family which generated the best score by the program, sortDist (807). The program, align2model was used to create an alignment between a successful hit and the

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SCOP sequence according to the SAM-T99 generated model (808). The alignments were then screened by identity scores and annotations created in XML database format (809). (pages 15-16, beginning on line 30 'Assigning annotations based on SCOP family with distsieve)

It is acknowledged the specification provides for five (5) specific criteria to be utilized in the selection of hits (i.e. hits to be kept), however, there does not appear to be support throughout the specification for the broad language of "a plurality of criteria" as encompassed by the instant claims (refer to the below 35 U.S.C. § 112 '*SCOPE OF ENABLEMENT*' and 35 U.S.C. § 112 2nd Paragraph '*VAGUE AND INDEFINITE*' rejections). Thus, new claims 82-105 are considered NEW MATTER.

SCOPE OF ENABLEMENT

Claims 82-105 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for five (5) specific criteria for selection of hits via the threshold curve analysis, does not reasonably provide enablement for all other criteria(s) for the selection of a plurality of hits.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 U.S.P.Q. 546 (B.P.A.I. 1986) and reiterated by the Court of Appeals in In re Wands, 8 U.S.P.Q. 2d 1400 at 1404 (C.A.F.C. 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable.

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While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instantly claimed invention broadly embraces “a plurality of criteria” beyond that which is taught and/or described by the specification. The specification discloses five (5) specific criteria for the selection of hits (refer to the above 35 U.S.C. § 112 1st Paragraph ‘*NEW MATTER*’ rejection for the cited portion of the specification). Thus, the specification provides limited guidance for the selection of “a plurality of hits based on a plurality of scores and a plurality of criteria”, wherein the selection of hits is based on a plurality of scores and the five (5) specific criteria of: 1) discarding hits when the E-values rise above a value of e-05 regardless of the other criteria; 2) keeping the first ten hits provided they score better than e-05; 3) automatically keeping the hits that more than 70% of the log of the maximum score; 4) using the point where the E-value plot drops abruptly or flattens as a threshold; and 5) keeping no more than a maximum number of hits (e.g., 1000). In the absence of additional guidance for the determination of “a plurality of criteria”, as broadly encompassed by the claims, one of skill in the art would be required to perform further undue experimentation for the refinement and subsequent determination of other criteria to be utilized with the “plurality of scores” for the selection of a “plurality of hits”. Applicants are directed to *Fields, Wilkinson, and Kende v. Conover and Woodward* [170 USPQ 276; How-to-Make Requirement section] which states:

"the description must place the invention in the possession of the public as fully as if the art or instrument itself had been practically and publicly employed. In order to accomplish this, it must be so particular and definite that from it alone, without experiment or the exertion of his own inventive skill, any person versed in the art to which it appertains could construct and use it."

Such independent decisions, judgments, tests, and validation are not considered to be routine experimentation and one of skill in the art practicing the invention would be required to use

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inventive skill to develop protocols for criteria determination and to utilized these identified criteria with the score for hit selection. No further guidance and/or direction is provided for the identification of "a plurality of criteria" as encompassed by the instant claims. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 82-105 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

VAGUE AND INDEFINITE

Claims 82, 90, 98, and all claims dependent therefrom recite the limitation "a plurality of criteria" which is considered vague and indefinite. The specification provides for five (5) specific criteria to be utilized with hit selection (refer to the above 35 U.S.C. 'NEW MATTER' rejection for the cited portion of the specification). However, the instant claims broadly encompass other criteria (i.e. plurality of criteria) beyond that disclosed in the specification and thus it is unclear what "a plurality of criteria" is intended to encompass. Clarification of the metes and bounds, via clearer claim language, is requested.

Claims Rejected Under 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 82, 84-87, 90, 92-95, 98, and 100-103 are rejected under 35 U.S.C. § 102(e) as being anticipated by Benner (U.S. Patent Number 6,377,893).

Benner et al. discloses methods for the utilization of models for the folded structure of a set of proteins from an evolutionary analysis of a set of aligned homologous protein sequences (Abstract). Models are generated based on structural relationships of proteins (i.e. information concerning three dimensional structure from conservation patterns)(instant claims 82, 90, & 98 “generation of a plurality of models”; Column 5, lines 14-22; Column 8, lines 29-49). The generated structure models are compared/searched with protein sequences to deduce the presence or absence of homology based on the presence or absence of structural similarity flanking key residue motifs in the polypeptide sequence (instant claims 82, 90, & 98 “inputting a plurality of protein sequences” and “determination of scores by comparison” of sequences with models; Abstract; Column 5, lines 58-67; Column 10, lines 10-23 and 34-42), wherein protein databases (i.e. 10000 families of proteins) are utilized (claims 84-86, 92-94, and 100-102 “50, 150, 500, etc. protein sequences”; Columns 12-13, lines 61-67 and 1-9, respectively). From the comparison proteins (i.e. hits) are selected for based on a scoring scheme (i.e. alignment) and set of criteria (instant claims 82, 90, & 98 “selection of hits” and claims 87, 95, & 103; Columns 5-6, lines 61-67 and 1-3, respectively; Column 23, lines 9-23). Identified proteins (i.e. hits) are assigned to the models (i.e. structural elements)(instant claims 82, 90, & 98 “assigning protein sequences”;

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Column 5, lines 23-26; Column 18, lines 18-20; Column 19, lines 59-65; Column 22, lines 29-31; Column 23, lines 23-30). Thus, Benner et al. anticipates the instantly claimed invention.

Claims Rejected Under 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicants are advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 82-87, 90-95, and 98-103 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Benner (U.S. Patent Number 6,377,893) taken in view of Eddy (Profile hidden Markov models. Bioinformatics. 1998, Volume 14, Number 9, pages 755-763).

Benner is herein applied from above (claims 82, 87, 90, 95, 98, and 103; refer to 35 U.S.C. § 102(e) Rejection). Benner indicates the utilization of a plurality of models in the disclosed invention (Column 5, lines 14-22).

Eddy et al. reviews the literature on profile hidden Markov model (HMM) methods and software (Abstract). The author indicates the application of hidden Markov models to time

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series, linear sequences, and modeling sequence families (i.e. motif-based HMMs) (instant claims 83, 91, and 99; page 755, right column, lines 9-31).

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the invention to practice Benner (U.S. Patent Number 6,377,893) in view of Eddy to utilize hidden Markov models as the plurality of structural models (i.e. motifs) in the method of utilizing models for the folded structure of a set of proteins from an evolutionary analysis of a set of aligned homologous protein sequences. Eddy indicates hidden Markov models can be used for aligning and scoring sequences to the model (page 756, left column, lines 38-41).

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify Applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables Applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Examiner Initials: *CSM*

Date: *February 6, 2005*

Ardin H. Marschel 2/6/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER